

Lindane - Impacts of the California Ban

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AOEC



Just One Lice is a Louse

I don't think lice are very nice.
They check in with their nits like your head is the Ritz
They come by the dozens and bring all their cousins.
They make your scalp itch
'til you scream like a witch
Every hair is a slide
where they can crawl down and hide
The nits cling to your roots
like mud clings to your boots.

by: Judith A. Goren

- Environmental health and children
 - Introduce basic concepts
- What can we learn from similar chemicals
 - PCBs, POPs, endocrine disruptors
- PBDEs (deca)
- Lindane
 - Potential health concerns
 - Children's susceptibility
 - Impacts of the California ban on pharmaceutical sales
 - Ethical issues

Unique Susceptibilities of Children

- Exploratory behavior
- Crawling
- Hand to mouth activity
- Restricted diet
- Teens – work, hobbies, high risk behaviors

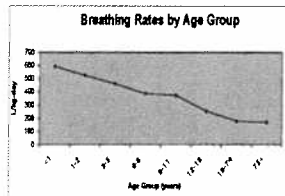


Physiologically differ :

- Still growing and developing
- Absorption, metabolism, & elimination different
- Blood-brain barrier still forming in young infants

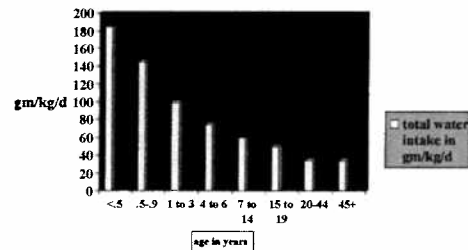
Increased Exposure from Inhalation and Dermal Absorption

- Increased metabolic rate
- Higher minute ventilation
 - Newborn 400 ml/min/kg
 - Adult 150 ml/min/kg
- Roughly double the surface area to body wt.
 - Increased absorption from dermal route



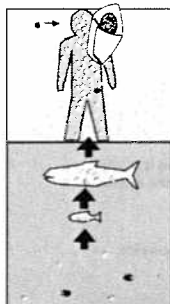
Miller M. et al., Int J Tox 2002

Higher Water Intake



Miller M. et al., Int J Tox 2002

Chemicals and the Food Chain (POPs)

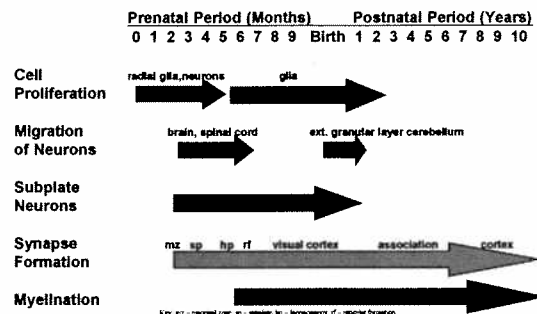


← Bioconcentration

← Biotransformation

← Persistence

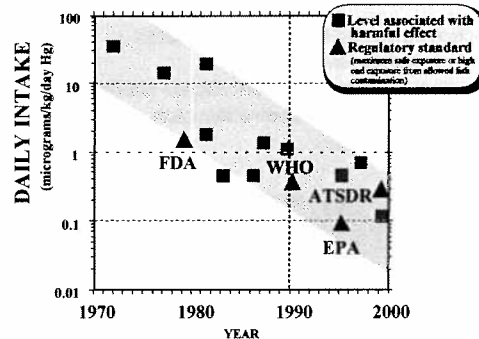
Time Lines of Developmental Processes in Humans



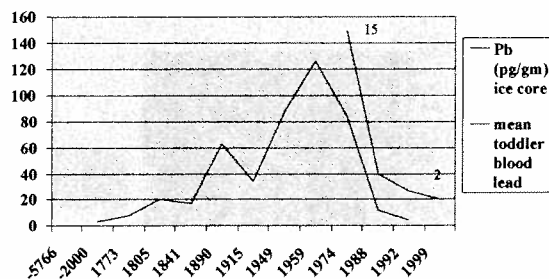
Specific processes disrupted by neurodevelopmental toxicants

proliferation	radiation, ethanol, <u>mercury</u> , cholinesterase inhibitors
migration	radiation, <u>mercury</u> , ethanol
differentiation	ethanol, nicotine, <u>mercury</u> , lead
synaptogenesis	radiation, ethanol, lead, triethyl tin, parathion, PCBs
gliogenesis & myelinization	dec. thyroid, ethanol, lead
apoptosis	ethanol, lead, <u>mercury</u>
signaling	ethanol, cholinesterase inhibitors, <u>mercury</u> , lead, PCBs

Mercury: Declining Threshold of Harm



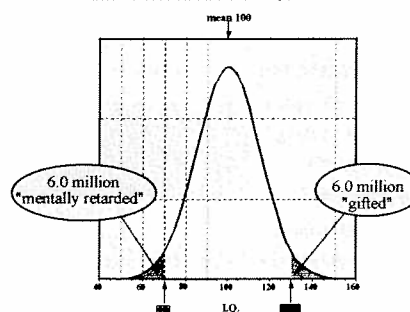
Greenland Snow and Ice Lead



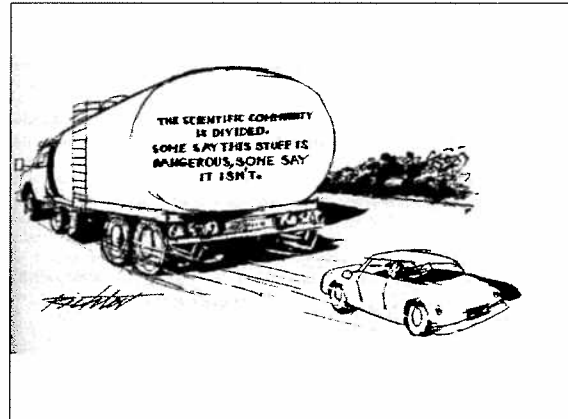
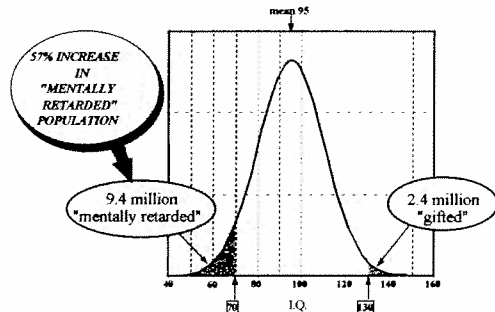
Derived from Candelone Et Al. 1995 J of Geophysical Research Vol.100 No. D8 and CDC, NHANES 2 and 3

The Significance of Small Effects: The Population Perspective

Effects of A Small Shift in IQ Distribution

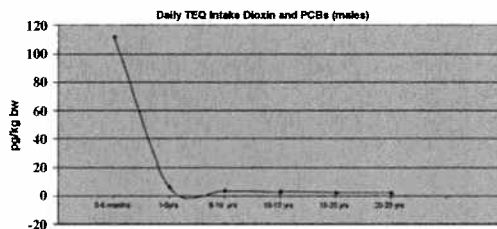


5 Point Decrease in Mean IQ



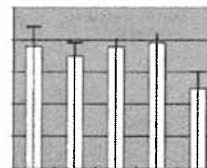
Fat Soluble Chemicals

Highest Intake in Breastfeeding infants



Source: Patandin et al, Environmental Health Perspectives, 107:1, 1999.

PCB exposure and 11 year IQ



- Decreases in word and reading comprehension, memory, attention
- Highest exposure group 3 times as likely to have low IQ and 2 times as likely to be 2 years behind in reading ability

Jacobsons (Wayne State U.)

Specific processes disrupted by neurodevelopmental toxicants

proliferation	radiation, ethanol, mercury, cholinesterase inhibitors, thyroid
migration	radiation, mercury, ethanol, thyroid
differentiation	ethanol, nicotine, mercury, lead, thyroid
synaptogenesis	radiation, ethanol, lead, triethyl tin, parathion, PCBs, thyroid
gliogenesis & myelination	ethanol, lead, thyroid
apoptosis	ethanol, lead, mercury
signaling	ethanol, cholinesterase inhibitors, mercury, lead, PCBs, thyroid (via laminin)

The PBDEs -- Flame Retardants



Use

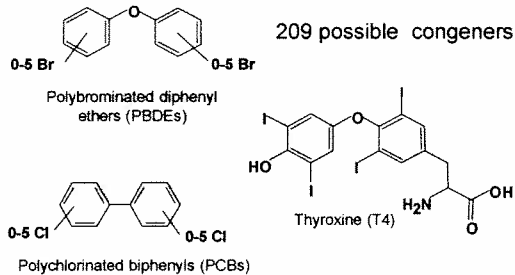
High-impact plastic
Foam cushions (furniture)
Textile coatings (drapes, furniture)
74.9 million pounds per year used in the Americas

• Toxicity concerns include

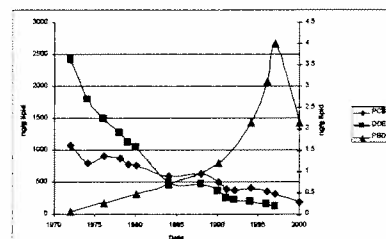
- highly bioaccumulative
- endocrine disruption
- altered behavior and learning (animal studies)

— LEVELS DO NOT APPEAR TO BE HIGHER IN ANGLERS (Moreland et al., 2005)

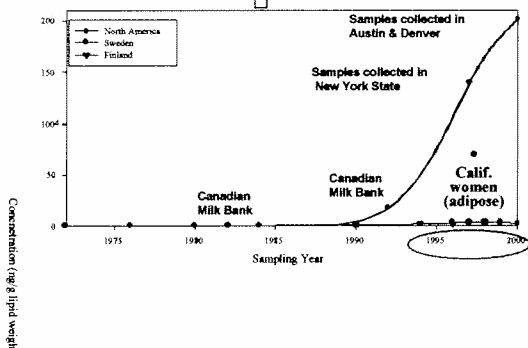
PCBs and PBDEs have similar structures



Organohalogens in Breastmilk (Sweden)



Concentrations of PBDEs in breast milk in "Breast Milk Bank Survey Project in the World"

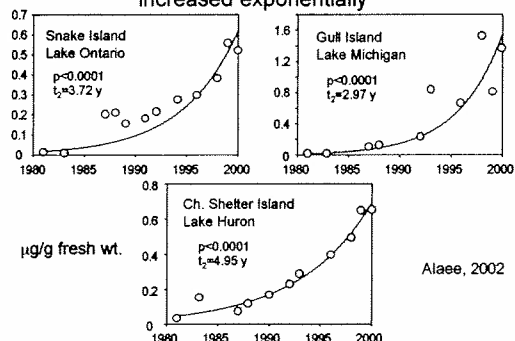


Metabolism of decaBDE

- decaBDE is absorbed, as much as >60% in some studies
- decaBDE metabolized by fish and mammals to nona, octa, hexa, and penta BDEs, including 153, 154, 183, 203, 206
- decaBDE or metabolites gets into brain
- Mice pups do not excrete PBDEs after single dose of BDE-47

Deborah Rice PhD

PBDEs in herring gull eggs in the Great Lakes have increased exponentially



Similar Findings in Rodents

- | PCB | PBDE |
|--|--|
| • Change in activity level | • Change in activity level |
| • Effects on learning and memory | • Effects on learning and memory |
| • Thyroid hormone production / transport | • Thyroid hormone production / transport |
| • Alter Ca ²⁺ homeostasis and neurotransmitters | • Alter Ca ²⁺ homeostasis and neurotransmitters |

When exposed to PCB and PBDE together neurodevelopmental effects noted at 1 tenth the dose and worsen with age

(Eriksson et al., SOT, 2003)

Characteristics of PCBs

• persistent in the environment and transported long distances
 • bioaccumulate and bioconcentrate up the food web
 • toxic

- carcinogenic
 - immunotoxic
 - endocrine disruptors (including thyroid)
 - developmental neurotoxins
 - developmental toxicants
 - reproductive toxicants
 - hepatotoxic
 - large database, including humans
- ♦ Banned in late 1970s

Characteristics of PBDEs

• persistent in the environment and transported long distances
 • bioaccumulate and bioconcentrate up the food web
 • toxic

- developmental neurotoxins
 - carcinogenic
 - endocrine disruptors (thyroid)
 - reproductive toxicants
 - hepatotoxic
 - limited database, animals
- ♦ Used beginning in 1970s
- ♦ penta and octa BDE commercial mixtures withdrawn in 2004

PBDEs may also have health effects in humans

- DecaBDE levels in breast milk predicted lower birth weight and length, smaller head circumference
- DecaBDE associated with decreased cycle length and decreased duration of menstrual bleeding
 - Deca predicted more adverse outcomes than other congeners
- PBDEs associated with cryptorchism
- Many effects in animals similar to PCBs
 - produce decreased IQ, attention deficits, and other neuropsychological problems

Chao *et al.*, 2006
Main *et al.*, 2007

decaBDE: A Cautionary Tale

- Assertion - deca not persistent or transported
 - Reality - transported long distances, degraded in the environment to toxic congeners
- Assertion - decaBDE will not be absorbed or bioconcentrate
 - Reality - decaBDE is absorbed, metabolites and possibly parent can bioconcentrate, present in human food chain
- Assertion - decaBDE is not toxic
 - Reality - may be largely true for parent compound based on *in vitro* studies
 - toxic to multiple systems *in vivo*
 - metabolites and degradation products are toxic

MMWR case report (June 3, 2005)

- 3 y/o boy ingested approximately 1 teaspoon of 1% lindane shampoo from used bottle
- Mother induces vomiting twice
- 1 hour later collapses and then has tonic-clonic seizure lasting 4-5 minutes
- Happy ending, released from ER later that day

WANTED



Head Lice AMERICAN ACADEMY OF PEDIATRICS

- 6 to 12 million infestations each year (US)
- Head lice are not a health hazard or a sign of uncleanliness and not responsible for the spread of any disease.
- The most common symptom is itching.
- Head lice are the cause of much embarrassment and misunderstanding

Pediatrics Volume 110, Number 3
September 2002, pp 638-643



Pediatrics Volume 110, Number 3
AMERICAN ACADEMY OF PEDIATRICS
Treatment

- Lindane (1%)
 - Organochloride that has central nervous system toxicity in humans
 - Low ovicidal activity (30% to 50% of eggs are not killed)
 - Resistance has been reported worldwide
 - For these reasons, it should be used very cautiously

Comparative *in vitro*
pediculicidal efficacy ... in US
Meinking et al, Archives of Dermatology, 2002

Product	killing 20 minutes	killing at 3 hours
Malathion	100%	100%
Natural pyrethrins (A200)	60%	82%
Permethrin	10%	84%
Lindane	2%	17%

Consistent findings in literature

- Clinical Inf Dis 2003;36(11):1355-1361
"... the availability of efficacious agents with more favorable safety profiles has virtually eliminated its [lindane's] use for lice treatment in the United States"
- Drugs 2001;61(8):1067-88
"permethrin... currently appears to have the best efficacy versus safety profile of topical treatments for scabies and lice."
- Skin Therapy Lett. 1999;5(1):1-3
"Permethrin is generally the treatment of choice for head lice and scabies, because of its residual effect."

Systematic Reviews from British Medical Journal – headlice (2003)

- Lindane
 - Found no RCTs comparing lindane versus placebo, other insecticides, mechanical removal of lice, or herbal treatments.
- Likely to be beneficial
 - Permethrin, Malathion
- Trade off
 - Trimethoprim-sulfamethoxazole
- Unknown effectiveness
 - Lindane, combinations of insecticides, herbals, mechanical removal



After this review some evidence in support of physical control

Health Hazards Associated with Lindane (human or animal evidence)

- Cancer
 - Human studies associated with leukemia, non-Hodgkins lymphoma, lung cancer. IARC/EPA possible human carcinogen, CA EPA human carcinogen (Prop. 65)
- Neurologic
 - Headaches, parasthesia, seizures (even when used correctly)
- Reproductive
 - Ovarian atrophy, embryotoxicity, decreases in sperm and testosterone
- Liver degeneration and cancer

The Young Particularly Sensitive to Some Effects

- Disruption of nerve transmission and brain function, blood cell formation, immune function, reproductive functions.
 - Perinatal exposure related to changes in heart electrical activity and degenerative lesions
- Labeled as a second line treatment to be used only after failure of other options (1995).
- In 2003, FDA advisory "Lindane should be used with caution for infants, children, the elderly, and individuals with ... skin conditions and in those who weigh < 110 lbs. as they may be at risk of serious neurotoxicity."

Alternatives to Lindane Through History



- ~5,600,000 BC Human head lice (*Pediculus humanus*) separated from Chimpanzee head lice (*Pediculus schaeffi*) about 5.6 million years ago.
- ~70,000 BC The separation of *P. humanus* into distinct "head" and "body" forms may have occurred 72,000 +/- 42,000 years ago
- ~3000 BC "Combing is the oldest method of lice control; nit combs have been found in Egyptian tombs."
- ~1240 Ibn Al-Baytar (13) wrote that honey "will kill lice if infested children's skin is painted with it."

Alternatives to Lindane Through History

- 1653 Robert Pemell suggests if only on head healthy to extract bad humors.
- 1681 Nicholas Culpeper "English tobacco" juice to kill lice on children's heads.
- ~1800 "Persian louse powder (Pyrethrum) was known to the Caucasus
- 1945 DDT (Dichloro-diphenyl-trichloroethane) was used by the U.S. forces in World War II to suppress lice and to delouse refugees
- 1954 Introduction of lindane (Kwell)
- 1970s Introduction of permethrin
- 1980s Introduction of malathion (Ovide)

•Promise of new methods

Fig. 1. An untreated head louse crawling on a hair strand (scale is at 10x magnification) (Magnification: x25.5)

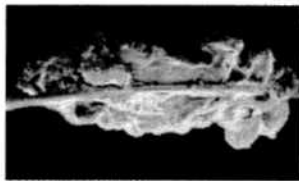


Fig. 2. A louse-treated head louse treated with DDT (scale is at 10x magnification) (Magnification: x27.5)

Perman, Ped 2004

Enactment of Ban



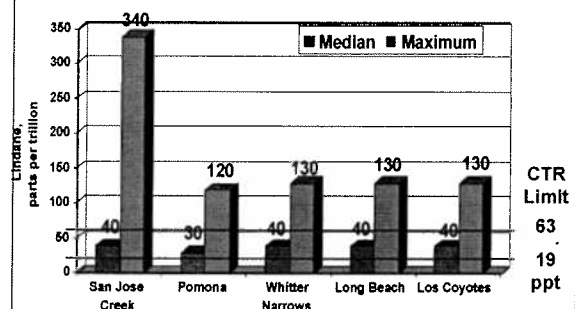
- Assembly Bill 2318
- California Health and Safety Code Section 111246
- "Commencing January 1, 2002, any product used for the treatment of lice or scabies in human beings that contains the pesticide Lindane shall not be used or sold in the state."
- No opposition on record to the bill

Los Angeles San calculates:

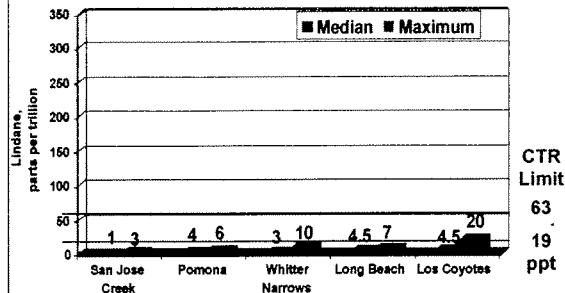


One treatment for head lice brings over 6 million gallons of water over the allowable discharge limits

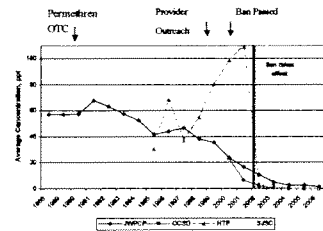
Lindane Leaving LACSD Water Reclamation Plants



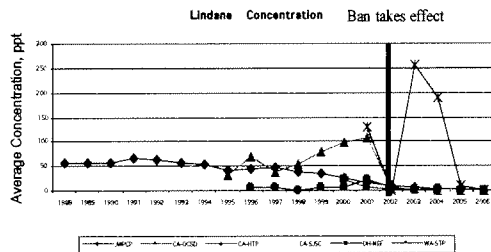
Lindane Leaving LACSD Water Reclamation Plants



Mean lindane concentrations: CA wastewater inflows



Mean lindane concentrations: Wastewater inflows (including Ohio post ban)



Clinical Impact - Anecdotal

"There haven't been any problems with not using lindane, and no calls for its return."

Dr. Gundala Dunne, California Department of Health Services, Infectious Disease Branch

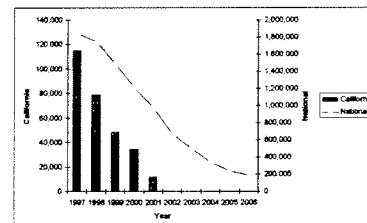
There have been no complaints regarding the ban and it was "not even a blip on the radar." Physicians "moved very smoothly and seamlessly into alternatives" and there are "other products that do the job just as effectively if used properly."

Carlo Michelotti, Chief Executive Officer, CA Pharmacists Association

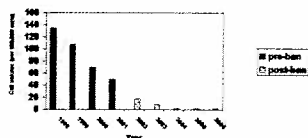
CA AAP member survey

- Random 400 active members n= 135 (171 responses, 43%)
- 61% of providers used lindane prior to ban
 - 94% report Rx change with ban
- 78% of providers did not notice any difficulty resulting from ban
- Of those who report any difficulty
 - 87% used lindane prior to the ban
 - More likely to be in solo practice and be in practice >15 yrs.
 - Increased resistance (97%); difficult to attribute to ban

Medi-Cal Prescriptions of Lindane (1997 through 2002) compared to nationwide prescriptions for years 1997-2006

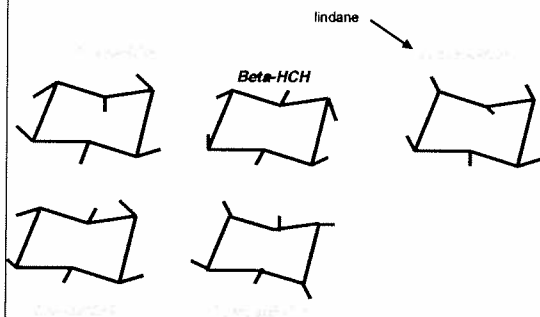


Annual calls to the CA Poison Control for lindane exposure



Erwin and White
The National Pediculosis Association, © Inc.
A Non-Profit Organization
Serving The Public Since 1983.

HCH consists of various isomers



Average composition of HCH obtained from the synthesis reaction

Compound	%
• Alpha-HCH	65-70
• Beta-HCH	7-9
• Gamma-HCH	14-15
• Delta-HCH	6-8
• Epsilon-HCH	1-2
• Other HCH isomers	0-1
• Benzene	0.5-5

What does this mean?

- For each ton lindane produced up to 10-12 tons of residuals were created that could not be used and became later hazardous waste
- Total prod. of lindane: 720.000 t (-1993)
- Total HCH residuals: 3-7 Million tons
 - Tot. prod HCH: 10 million tons -1948-1997

1975

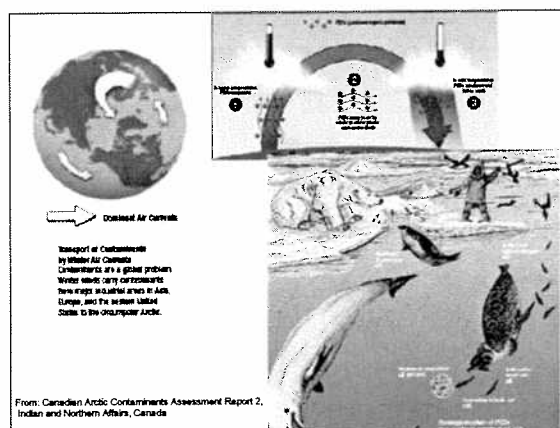




Desolated factory with HCH waste inside



Inside the former factory 1992



What are the implications of lindane use in the US?

- Alternatives are available
- Long range transport
 - Largest US and Canadian arctic sources likely come from Asia
 - Toxic legacy left with those least able to deal with it
- Should pharmaceutical use be banned?

Demand for PBDEs is highest in Americas
metric tons, 2003

